DETAILED ACTION

Status of the Application

This Office Action is in response to applicant's arguments filed on 5/8/2008. Claims 3-4 has been cancelled. Claims 1-2, 5-21 are pending. Claim 1 has been amended. Claim 21 has been withdrawn. Claims 1-2, 5-20 are examined herein.

At the outset, there are a couple of issues regarding the last Office Action filed on 2/8/2008 that need to be addressed. Firstly, the RCE filed on 10/26/2007 was not properly acknowledged, therefore it is acknowledged in this Office Action instead. Secondly, the last Office Action was mistakenly made Final instead of Non-Final, therefore the finality of the last Office Action is now vacated. In summary, the last Office Action filed on 2/28/2008 will be treated as a Non-Final Office Action, acknowledging the RCE filed on 10/26/2007. The attorney has been made aware of this misunderstanding in the attached Interview Summary.

Applicant's arguments and amendments have necessitated the withdrawal of all 112 rejections of the last Office Action. Applicant's arguments with respect to the 103(a) rejections of the last Office Action have been fully considered but found not persuasive. The 103(a) rejections of the last Office Action are maintained for reasons of record and modified or repeated below for Applicant's convenience.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-2, 5-12, 14-18, 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over TAP Report 1 ("Photodynamic Therapy of Subfoveal Choroidal Neovascularization in Age-related Macular Degeneration with Verteporfin." Arch Ophtalmol. 1999; 117:1329-1345) (the TAP Report).

The instant claims are directed to methods of treating an occult choroidal neovascular (CNV) lesion comprising administering photodynamic therapy to a subject having Occult CNV, wherein the subject is assessed as having either or both (a) a small lesion with a size less than about 4-5 disc areas or (b) poor visual acuity of less than about 65 letters prior to treatment and wherein the occult lesion comprise an occult component of >50% to <100% of the lesion.

The TAP Report teaches the instantly claimed method. Tap Report teaches methods of administering verteporfin, a green porphyrin (which is also known as BPD-MA, see Reg Number 129497-78-5) to patients suffering from Occult CNV. (see page 1330 under the heading Patient Selection, last para.). Out of the 402 Patients in the Vertoporfin arm of the study, at least 305 patients had evidence of Occult CNV (see Table 2 at page 1334, last criteria under the category Evidence of Occult CNV). Further, out of the same 402 patients at least 199 patients had a visual acuity of less than 53 letters (see Table 2, Vertoporfin Arm, under the category Visual Acuity criteria). Thus, at least about 100 patients who had received a photodynamic regimen of verteporfin, had evidence of Occult CNV with visual acuity of less than 65.

Further, Table 5 shows benefit from verteporfin therapy on patients with ≥50% classic CNV (or ≤50% occult CNV). Furthermore, the upper limit of the claimed invention (99% occult CNV) is also obvious because of the teaching that "the subgroup with no classic CNV (100% occult CNV) had a large treatment benefit" from pg. 1339 of the TAP Report.

Examiner also states that among the population in the Verteporfin Arm, 259 appear to have lesion size of less than 6 disc areas (see page 1335, table 2, under Vertoporfin Arm, Under the Area of Lesion, MPS Disc Areas criteria). Therefore, the population who showed Occult CNV in the TAP Report and further received verteporfin, are the same as the instantly claimed population. Said population received an aqueous Verteprofin solution in amount of about 6 mg/m^2 (see abstract, also page 1332, at 1st col). Fifteen minutes after administration of the Verteprofin the CNV lesions were

irradiated with a laser light for about 83 seconds in a light exposure of 50 J/cm^2. (see col 1 page 1332). Accordingly, the limitations of claims 14-18 are met.

All method steps of the instantly claimed process are described for the population who showed Occult CNV prior to the therapy in the TAP Report Verteporfin Arm. Accordingly, the instantly claimed intended purpose is inherently achieved in the said population.

Applicant is also informed that the recitation of 45% efficacy of therapy in Occult CNV group, as recited in page 1338 is not a teaching away, because such conclusion does not mean that no patient has benefited from the methodology described in Vertopoifin Arm of the TAP Report. Rather, such percentage is only viewed as a comparison to the control group. Examiner adds that the 33.1% of the TAP Report's Verteporfin Arm included lesion. TAP Report only fails to explicitly state that the patients in the Verteporfin Arm of the study had an occult component of >50% to <100% of the lesion.

Nevertheless, absent a showing of unexpected results or evidence to the contrary, it would have been obvious to one of ordinary skill in the art at the time of invention to practice the method steps of TAP Report to treat patients with occult CNV lesion having an occult component of >50% to <100% of the lesion, because as shown by the Report, one of ordinary skill in the art would have had a reasonable expectation of success to observe some degree of improvement in ocular condition of the patients suffering from said occult CNV.

Claims 13 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over the TAP Report as applied to claims 1-2, 5-12, 14-18, 20 in view of Zeimer (US Patent 5,935,942).

The teachings of the TAP report are described above. The TAP report only fails to specifically describe attachment the use of a targeting ligand and the dosing of its photosensitizer per body weight of subjects.

Zeimer is used to describe the same process as in TAP report except that the photosensitizer is encapsulated or coupled with a targeting or tissue specific agent (see col 12, lines 28-50; col 14, lines 15-col 24). The process of Zeimer employs targeted liposomes (col 25-26) for patients having Occult CNV.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to add a targeting agent, such as an antibody, to the photosensitizer employed in TAP report, because as suggested by Zeimer, the ordinary skill in the art would have had a reasonable expectation of success in improving the clinical outcome.

Further, absent a showing of criticality, it would have been obvious to one of ordinary skill in the art at the time of invention to optimize the dosing ranges of the photosensitizer in TAP report by routine experimentation and express it based on the body weight of subjects.

Response to Arguments

Applicant argues against Examiner's interpretation of the Tap Report 1, particularly the claimed subgroup being inherently located in the verteporfin-treatment

population. Applicant respectfully submit that because certain patients having poor visual acuity and/or small lesion size also have some evidence of occult CNV does not necessarily mean that such patients fell within the scope of the claims. Moreover, the Examiner's conclusions ignores the express teachings of the Tap Report 1 that occult lesions, and particularly lesions having between >50% and <100% occult character, are non-responsive to PDT treatment with verteporfin. Applicant points to where the TAP Report explicitly teaches that patients with greater than 50% to less than 100% occult CNV achieved no benefit from verteporfin PDT therapy. Applicant points to Table 5 (pg. 1340) in the Tap Report 1, where there was no significant differential between verteporfin-treated patients and placebo-treatment group. Applicant point to the author's conclusion that "no appreciable difference was observed in the group of patients with lesions in which the area of classic CNV was greater than 0% but less than 50% of the area of the entire lesion at baseline."

This is not persuasive because the results that there was no benefit from verteporfin therapy in Table 5 only refers to the subset of patients with >0 to <50% classic CNV (or >50 to <100% occult CNV). However, there is no denying the large benefit of verteporfin in the subset of patients with ≥50% of classic CNV (or ≤50% occult CNV) as disclosed also in Table 5. So, the data can infer that a patient with 50% occult CNV benefits from verteporfin therapy. Therefore, it would be obvious to administer verteporfin therapy to a patient with 51% occult CNV due to routine experimentation and optimization. Furthermore, the upper limit of the claimed invention (99% occult CNV) is

also obvious because of the teaching that "the subgroup with no classic CNV (100% occult CNV) had a large treatment benefit" from pg. 1339 of the TAP Report.

Applicant is reminded that the standard for obviousness is not absolute but a reasonable expectation of success. In this manner, it is obvious to experiment with a subgroup of patients on the outer limits of the claimed range of ≥50 to ≤100% occult CNV. Therefore, absent a teaching of unexpected results or the criticality of the claimed range, it is obvious over the cited prior art.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

YSC

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1617